Hemorrhagic Fevers (Viral)
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Hemorrhagic Fevers (Viral)

Overview [1,2]

Viral hemorrhagic fever (VHF) is a general term for illnesses caused by members of several different viral families. Most of the viruses causing this illness are restricted in their geographic range by the limitations of their natural host species, which are usually rodents or insects. The host species for Ebola and Marburg are unknown, but these viruses also appear to have limited ranges. Some viruses, in particular dengue, are less limited in their geographic ranges.[1,2,3] It is essential for rapid diagnosis and management that a travel history is obtained from the patient.

This section will focus on those viruses that initially present with similar symptoms and may progress to more severe forms of illness, including Ebola, Marburg, Lassa, Crimean-Congo Hemorrhagic Fever (CCHF), Dengue and the South American hemorrhagic fevers: Argentine, Bolivian and Venezuelan. Viral candidates for illnesses similar to VHF, Hantavirus and yellow fever, are discussed in separate sections of this manual.

For a complete description of Viral Hemorrhagic Fevers, refer to the following texts:
- Control of Communicable Diseases Manual (CCDM).
- Red Book, Report of the Committee on Infectious Diseases.

NOTE: Some of the VHFs are potential bioterrorism weapons. **If the case has no remarkable travel history, a bioterrorism event should be considered.** If you suspect that you are dealing with a bioterrorism situation, contact your Regional Communicable Disease Coordinator immediately.

Case Definition – Dengue Fever and Dengue Hemorrhagic Fever [3]

Clinical description
An acute febrile illness characterized by frontal headache, retro-ocular pain, muscle and joint pain, and rash. The principal vector is the *Aedes aegypti* mosquito and transmission usually occurs in tropical or subtropical areas. Severe manifestations (e.g., dengue hemorrhagic fever and dengue shock syndrome) are rare but may be fatal.

Laboratory criteria for diagnosis
- Isolation of dengue virus from serum and/or autopsy tissue samples, or
- Demonstration of a fourfold or greater rise or fall in reciprocal immunoglobulin G (IgG) or immunoglobulin M (IgM) antibody titers to one or more dengue virus antigens in paired serum samples, or
- Demonstration of dengue virus antigen in autopsy tissue or serum samples by immunohistochemistry or by viral nucleic acid detection.

Case Classification
Confirmed: a clinically compatible case that is laboratory confirmed.
Probable: a clinically compatible case with supportive serologic findings (a reciprocal IgG antibody titer of $\geq$ 1280 or a positive IgM antibody test on a single acute (late)- or convalescent-phase serum specimen to one or more dengue virus antigens.

Comment
Dengue hemorrhagic fever is defined as an acute febrile illness with minor or major bleeding phenomena, thrombocytopenia ($\leq$ 100,000/mm^3), and evidence of plasma leakage documented by hemoconcentration (hematocrit increased by $\geq$ 20%) or other objective evidence of increased capillary permeability. The definition of dengue shock syndrome follows all of the above criteria for dengue hemorrhagic fever and also includes hypotension or narrow pulse pressure ($\leq$ 20 mm Hg).

Case Definition – South American Hemorrhagic Viral, Lassa, Ebola Hemorrhagic, Marburg Hemorrhagic, and Crimean-Congo Hemorrhagic Fevers [(4)]

No national case definitions have been developed. For surveillance in Missouri, the following definitions should be used.

Clinical description
Initial symptoms are non-specific and generally include either an acute or insidious onset of progressive fever, myalgia, headache and sometimes sore throat. This may be followed by vomiting, diarrhea, conjunctivitis, petechiae, reduced renal and hepatic functions, and both internal and external bleeding. Case fatality rates for hospitalized patients have ranged from 15% for Lassa fever to 90% for Ebola-Zaire.

Laboratory criteria for diagnosis
Laboratory diagnosis may be made by any of the following procedures:
- Isolation of the virus by cell culture
- Detection of viral RNA by use of PCR
- Detection of viral antigens by use of antigen-capture EIA
- Detection of IgM antibodies to the virus
- Detection of a fourfold rise in antibodies between acute and convalescent serum.

Case classification
Confirmed: a case that is laboratory confirmed
Probable: a clinically compatible case that is epidemiologically linked to a confirmed case.
Suspect: a clinically compatible case.

Information Needed for Investigation

Verify the diagnosis. What laboratory tests were conducted? What were the results? What laboratory conducted the testing and what is their phone number? If laboratory tests were not conducted, are specimens available? What are the patient's clinical symptoms? What is the name and phone number of the attending physician?
Determine if the case had a history of recent foreign travel. VHFs are not endemic diseases in North America and one case is considered an outbreak.
Establish the extent of illness. Determine if household, traveling companions, worksite contacts, or other close contacts are, or have been, ill by contacting the health care provider, patient, family member, traveling companions, or employer.
Contact the Regional Communicable Disease Coordinator immediately upon notification of a suspected or confirmed case.

Case/Contact Follow Up And Control Measures

Determine the source of infection:

- For the three weeks prior to onset of illness, determine the case's travel history in detail, including airline flight numbers and times, cruise ships, and tour groups. Determine the countries, cities, and villages visited, the dates they were visited and how long the case stayed there. Determine the case's traveling accommodations including dates of stay. Determine the case's activities during the period of travel.
- Determine the occupation and specific job duties of the case. Does the case work in a laboratory? Does the case work with animals in any capacity? Does the case work in a medical capacity?

Control Measures

See the Control of Communicable Diseases Manual, viral hemorrhagic fever sections, "Methods of control."

See the Red Book, viral hemorrhagic fever sections, "Control Measures."

Laboratory Procedures

Specimens: [(4)]

The State Public Health Laboratory (SPHL) does not perform VHF testing. However, the SPHL must be notified when VHF specimens are sent to CDC for testing. Many of the agents of VHF are biosafety level (BSL)-4 agents and should only be examined in a BSL-4 laboratory. Only specimens essential for diagnosis or monitoring should be collected and strict universal precautions must be used during collection. In addition, special precautions must be taken when transporting these specimens. Information on laboratory procedures can be obtained from the Regional Communicable Disease Coordinator or from staff at the SPHL. The SPHL web site is: http://www.dhss.state.mo.us/Lab/index.htm. (22 May 2003)

The following information is provided as a reference:

1. Ten milliliters of clotted venous blood should be placed in a sealed plastic container. Needles should not be recapped, bent, broken, removed from disposable syringes, or otherwise handled. Blood-taking equipment should be put in a rigid plastic container filled with disinfectant solution and autoclaved or incinerated.
2. Midstream urine specimens should be collected by clean catch. Five milliliters of urine should be put in a plastic screw-cap container with one of the following: rabbit serum albumin diluted to a final concentration of 25%, human serum albumin diluted to a 1% concentration, or bovine serum albumin at a final concentration of 10%.
3. Throat swabs should be placed in plastic screw-cap containers in 1 mL of sterile, phosphate-buffered neutral saline containing 25% rabbit serum, 1% human serum albumin, or 10% bovine serum albumin.

Reporting Requirements

Viral hemorrhagic fevers are Category IB reportable diseases and shall be reported to the local health authority or to the Missouri Department of Health and Senior Services (DHSS) within 24 hours of first knowledge or suspicion by telephone, facsimile or other rapid communication. **A single case of any viral hemorrhagic fever constitutes an outbreak of public health concern.**

1. For confirmed, probable, and suspect cases complete a “Disease Case Report” (CD-1).
2. For all cases, complete a “Record of Investigation of Communicable Disease” (CD-2).
3. Entry of the completed CD-1 into the MOHSIS database negates the need for the paper CD-1 to be forwarded to the Regional Health Office.
4. Send the completed secondary investigation form to the Regional Health Office.
5. All outbreaks or “suspected” outbreaks must be reported as soon as possible (by phone, fax, or e-mail) to the Regional Communicable Disease Coordinator. This can be accomplished by completing the Missouri Outbreak Surveillance Report (CD-51).

6. Within 90 days from the conclusion of an outbreak, submit the final outbreak report to the Regional Communicable Disease Coordinator.

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2. Shope, Robert E. and James M. Meegan. "African Hemorrhagic Fevers Caused by Marburg and Ebola Viruses." and Jahrling, Peter B. "Arenaviruses." Viral Infections of Humans Epidemiology and Control; 4th ed. Eds. Alfred S. Evans and Richard A. Kaslow. New York: Plenum, 1997: 139-150. 185-209.
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Arenaviridae: Including South American Hemorrhagic Viral Fevers

What are the Arenaviridae?

The Arenaviridae are a family of viruses whose members are generally associated with rodent-transmitted disease in humans. Each virus usually is associated with a particular rodent host species in which it is maintained. Arenavirus infections are relatively common in humans in some areas of the world and can cause severe illnesses. The virus particles are spherical and have an average diameter of 110-130 nanometers. All are enveloped in a lipid (fat) membrane. Viewed in cross-section, they show grainy particles that are ribosomes acquired from their host cells. It is this characteristic that gave them their name, derived from the Latin "arena," which means "sandy." Their genome, or genetic material, is composed of RNA only, and while their replication strategy is not completely understood, we know that new viral particles, called virions, are created by budding from the surface of their hosts' cells.

When were the members of this virus family recognized?

The first arenavirus, lymphocytic choriomeningitis virus (LCMV), was isolated in 1933 during a study of an epidemic of St. Louis encephalitis. Although not the cause of the outbreak, LCMV was found to be a cause of aseptic (non-bacterial) meningitis. By the 1960s, several similar viruses had been discovered and they were classified into the new family Arenaviridae. Since Tacaribe virus was found in 1956, new arenaviruses have been discovered on the average of every one to three years. A number of arenaviruses cause hemorrhagic disease. Junin virus, isolated in 1958, was the first of these to be recognized. This virus causes Argentine hemorrhagic fever in a limited agricultural area of the pampas in Argentina. Several years later, in 1963, in the remote savannas of the Beni province of Bolivia, Machupo virus was isolated. The next member of the virus family to be associated with an outbreak of human illness was Lassa virus in Africa in 1969. Most recently, Guanarito and Sabia viruses were added to this family.

What viruses are included in the virus family?

The arenaviruses are divided into two groups: the New World or Tacaribe complex and the Old World or LCM/Lassa complex. Viruses in these groups that cause illness in humans are as follows:

Virus	Disease
Lymphocytic choriomeningitis virus	Lymphocytic choriomeningitis
Lassa virus	Lassa fever
Junin virus	Argentine hemorrhagic fever

Machupo virus	Bolivian hemorrhagic fever
Guanarito virus	Venezuelan hemorrhagic fever
Sabia	As yet unnamed (found in Brazil)

What kinds of animal hosts do these viruses have?

These viruses are zoonotic, meaning that, in nature, they are found in animals. Each virus is associated with either one species or a few closely related rodents, which constitute the virus' natural reservoir. Tacaribe complex viruses are generally associated with the New World rats and mice (family Muridae, subfamily Sigmodontinae). The LCM/Lassa complex viruses are associated with the Old World rats and mice (family Muridae, subfamily Murinae). Taken together, these types of rodents are located across the greater proportion of the earth's landmass, including Europe, Asia, Africa, and the Americas. One notable exception is Tacaribe virus, found in Trinidad, which was isolated from a bat.

How are arenaviruses spread?

The rodent hosts of arenaviruses are chronically infected with the viruses; however, the viruses do not appear to cause obvious illness in them. Some Old World arenaviruses appear to be passed from mother rodents to their offspring during pregnancy, and thus remain in the rodent population generation after generation. Some New World arenaviruses are transmitted among adult rodents, likely via fighting and inflicting bites. Only a portion of the rodents in each host species is infected at any one time, and in many cases only in a limited portion of the host's geographical range. The viruses are shed into the environment in the urine or droppings of their infected hosts. Human infection with arenaviruses is incidental to the natural cycle of the viruses and occurs when an individual comes into contact with the excretions or materials contaminated with the excretions of an infected rodent, such as ingestion of contaminated food, or by direct contact of abraded or broken skin with rodent excrement. Infection can also occur by inhalation of tiny particles soiled with rodent urine or saliva (aerosol transmission). The types of incidental contact depend on the habits of both humans and rodents. For example, where the infected rodent species prefers a field habitat, human infection is associated with agricultural work. In areas where the rodent species' habitat includes human homes or other buildings, infection occurs in domestic settings. Some arenaviruses, such as Lassa and Machupo viruses, are associated with secondary person-to-person and nosocomial (health-care setting) transmission. This occurs when a person infected by exposure to the virus from the rodent host spreads the virus to other humans. This may occur in a variety of ways. Person-to-person transmission is associated with direct contact with the blood or other excretions, containing virus particles, of infected individuals. Airborne transmission has also been reported in connection with certain viruses. Contact with objects contaminated with these materials, such as medical equipment, is also associated with transmission. In these situations, use of protective clothing and disinfection procedures (together called "barrier nursing") help prevent further spread of illness.

Adapted from: 2002, Special Pathogens Branch, Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Public Health Service, U.S. Department of Health and Human Services.
http://www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/arena.htm (20 May 2003)

Arenaviridae: Lassa Fever

What is Lassa fever?

Lassa fever is an acute viral illness that occurs in West Africa. The illness was discovered in 1969 when two missionary nurses died in Nigeria, West Africa. The cause of the illness was found to be Lassa virus, named after the town in Nigeria where the first cases originated. The virus, a member of the virus family Arenaviridae, is a single-stranded RNA virus and is zoonotic, or animal-borne. In areas of Africa where the disease is endemic (that is, constantly present), Lassa fever is a significant cause of morbidity and mortality. While the disease is mild or has no observable symptoms in about 80% of people infected with the virus, the remaining 20% have a severe multisystem disease. Lassa fever is also associated with occasional epidemics, during which the case-fatality rate can reach 50%.

Where is Lassa fever found?

Lassa fever is an endemic disease in portions of West Africa. It is recognized in Guinea, Liberia, Sierra Leone, as well as Nigeria. However, because the rodent species, which carry the virus, are found in other regions outside of West Africa, the actual geographic range of the disease may extend to other portions of Africa.

How many people become infected?

The number of Lassa virus infections per year in West Africa is estimated at 100,000 to 300,000, with approximately 5,000 deaths. Unfortunately, such estimates are crude, because surveillance for cases of the disease is not uniformly performed. In some areas of Sierra Leone and Liberia, it is known that 10%-16% of people admitted to hospitals have Lassa fever, which indicates the serious impact of the disease on the population of this region.

In what animal host is Lassa virus maintained?

The reservoir, or host, of Lassa virus is a rodent known as the "multimammate rat" of the genus *Mastomys*. It is not certain which species of *Mastomys* are associated with Lassa; however, at least two species carry the virus in Sierra Leone: *M. huberti* and *M. erythroleucus*. *Mastomys* rodents breed very frequently, produce large numbers of offspring, and are numerous in the savannas and forests of West, Central, and East Africa. In addition, some species, like *M. huberti*, prefer to live in human homes. All these factors together contribute to the relatively efficient spread of Lassa virus from infected rodents to humans.

How do humans get Lassa fever?

There are a number of ways in which the virus may be transmitted, or spread, to humans. The *Mastomys* rodents shed the virus in urine and droppings. Therefore, the virus can be transmitted through direct contact with these materials, through touching objects or eating food contaminated with these materials, or through cuts or sores. Because *Mastomys* rodents often live in and around homes and scavenge on human food remains or poorly stored food, transmission of this sort is common. Contact with the virus also occurs when a person inhales tiny particles in the air contaminated with rodent excretions. This is called aerosol or airborne transmission. Finally, because *Mastomys* rodents are sometimes used as a food source, infection may occur via direct contact when they are caught and prepared for food. Lassa fever may also spread through person-to-person contact. This type of transmission occurs when a person comes into contact with virus in the blood, tissue, secretions, or excretions of an individual infected with the Lassa virus. A person may also become infected by breathing in small airborne particles, which an already infected person may produce by actions like coughing. The virus cannot be spread through casual contact (including skin-to-skin contact without exchange of body fluids). Person-to-person transmission is common in both village settings and in health care settings, where, along with the above-mentioned modes of transmission, the virus also may be spread in contaminated medical equipment, such as reused needles (this is called “nosocomial” transmission).

What are the symptoms of Lassa fever?

Symptoms of Lassa fever typically occur 1-3 weeks after the patient comes into contact with the virus. These include fever, retrosternal pain (pain behind the chest wall), sore throat, back pain, cough, abdominal pain, vomiting, diarrhea, conjunctivitis, facial swelling, proteinuria (protein in the urine), and mucosal bleeding. Neurological symptoms have also been described, including hearing loss, tremors, and encephalitis. Because the symptoms of Lassa fever are so varied and nonspecific, clinical diagnosis is often difficult.

How is the disease diagnosed in the laboratory?

Lassa fever is most often diagnosed by using enzyme-linked immunosorbent serologic assays (ELISA), which detect IgM and IgG antibodies as well as Lassa antigen. The virus itself may be cultured in 7 to 10 days. Immunohistochemistry performed on tissue specimens can be used to make a post-mortem diagnosis. The virus can also be detected by reverse transcription-polymerase chain reaction (RT-PCR); however, this method is primarily a research tool.

Are there complications after recovery?

The most common complication of Lassa fever is deafness. Various degrees of deafness occur in approximately one-third of cases, and in many cases hearing loss is permanent. As far as is known, severity of the disease does not affect this complication: deafness may develop in mild as well as in severe cases. Spontaneous abortion is another serious complication.

What proportion of people die from the illness?

Approximately 15%-20% of patients hospitalized for Lassa fever die from the illness. However, overall only about 1% of infection with the Lassa virus result in death. The death rates are particularly high for women in the third trimester of pregnancy, and for fetuses, about 95% of which die in the uterus of infected pregnant mothers.

How is Lassa fever treated?

Ribavirin, an antiviral drug, has been used with success in Lassa fever patients. It has been shown to be most effective when given early in the course of the illness. Patients should also receive supportive care consisting of maintenance of appropriate fluid and electrolyte balance, oxygenation and blood pressure, as well as treatment of any other complicating infections.

What groups are at risk for getting the illness?

Individuals at risk are those who live or visit areas with a high population of *Mastomys* rodents infected with Lassa virus or are exposed to infected humans. Hospital staff are not at great risk for infection as long as protective measures are taken.

How is Lassa fever prevented?

Primary transmission of the Lassa virus from its host to humans can be prevented by avoiding contact with *Mastomys* rodents, especially in the geographic regions where outbreaks occur. Putting food away in rodent-proof containers and keeping the home clean help to discourage rodents from entering homes. Using these rodents as a food source is not recommended. Trapping in and around homes can help reduce rodent populations. However, the wide distribution of *Mastomys* in Africa makes complete control of this rodent reservoir impractical. When caring for patients with Lassa fever, further transmission of the disease through person-to-person contact or nosocomial routes can be avoided by taking preventive precautions against contact with patient secretions (together called VHF "isolation precautions" or "barrier nursing methods"). Such precautions include wearing protective clothing, such as masks, gloves, gowns, and goggles; using infection control measures, such as complete equipment sterilization; and isolating infected patients from contact with unprotected persons until the disease has run its course.

What needs to be done to address the threat of Lassa fever?

Further educating people in high-risk areas about ways to decrease rodent populations in their homes will aid in the control and prevention of Lassa fever. Other challenges include developing more rapid diagnostic tests and increasing the availability of the only known drug treatment, ribavirin. Research is presently under way to develop a vaccine for Lassa fever.

Adapted from: 2002, Special Pathogens Branch, Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Public Health Service, U.S. Department of Health and Human Services.
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Filoviridae: Ebola Hemorrhagic Fever

What is Ebola hemorrhagic fever?

Ebola hemorrhagic fever is a severe, often fatal disease in humans and nonhuman primates (monkeys and chimpanzees) that has appeared sporadically since its initial recognition in 1976. The disease is caused by infection with Ebola virus, named after a river in the Democratic Republic of the Congo (formerly Zaire) in Africa, where it was first recognized. The virus is one of two members of a family of RNA viruses called the Filoviridae. Three of the four species of Ebola virus identified so far have caused disease in humans: Ebola-Zaire, Ebola-Sudan, and Ebola-Ivory Coast. The fourth, Ebola-Reston, has caused disease in nonhuman primates, but not in humans.

Where is Ebola virus found in nature?

The exact origin, locations and natural habitat (known as the "natural reservoir") of Ebola virus remain unknown. However, on the basis of available evidence and the nature of similar viruses, researchers believe that the virus is zoonotic (animal-borne) and is normally maintained in an animal host that is native to the African continent. A similar host is probably associated with the Ebola-Reston species isolated from infected cynomolgous monkeys that were imported to the United States and Italy from the Philippines. The virus is not known to be native to other continents, such as North America.

Where do cases of Ebola hemorrhagic fever occur?

Confirmed cases of Ebola hemorrhagic fever have been reported in the Democratic Republic of the Congo, Gabon, Sudan, and the Ivory Coast. An individual with serologic evidence of infection but showing no apparent illness has been reported in Liberia, and a laboratory worker in England became ill as a result of an accidental needlestick. No case of the disease in humans has ever been reported in the United States. Ebola-Reston virus caused severe illness and death in monkeys imported to research facilities in the United States and Italy from the Philippines; during these outbreaks, several research workers became infected with the virus, but did not become ill. Ebola hemorrhagic fever typically appears in sporadic outbreaks usually spread within a health care setting (a situation known as “amplification”). It is likely that sporadic, isolated cases occur as well, but go unrecognized.

How is Ebola virus spread?

Infection with Ebola virus in humans is incidental - humans do not "carry" the virus. Because the natural reservoir of the virus is unknown, the manner in which the virus first appears in a human at the start of an outbreak has not been determined. However, researchers have hypothesized that the first patient becomes infected through contact with an infected animal. After the first case patient in an outbreak setting (often called the "index case") is infected, humans can transmit the virus to each other in several ways. People can be exposed to Ebola virus from direct contact with the blood and/or secretions of an infected person. This is why the virus has often been spread through the families and friends of infected persons: in the course of feeding, holding or otherwise caring for them, family members and friends would come into close contact with such secretions. People can also be exposed to Ebola virus through contact with objects, such as needles, that have been contaminated with infected secretions. Nosocomial transmission has been associated frequently with Ebola outbreaks. It includes both types of transmission described above, but it is used to describe the spread of disease in a health care setting such as a clinic or hospital. In African health care facilities, patients are often cared for without the use of a mask, gown, or gloves, and exposure to the virus has occurred when health care workers treated individuals with Ebola hemorrhagic fever without wearing these types of protective clothing. In addition, when needles or syringes are used, they may not be of the disposable type, or may not have been sterilized, but only rinsed before re-insertion into multi-use vials of medicine. If needles or syringes become contaminated with virus and are then reused, numbers of people can become infected. The Ebola-Reston virus species that appeared in a primate research facility in Virginia may have been transmitted from monkey to monkey through the air in the facility. While all Ebola virus species have displayed the ability to be spread through airborne particles (aerosols) under research conditions, this type of spread has not been documented among humans in a real world setting, such as a hospital or household.

What are the symptoms of Ebola hemorrhagic fever?

The signs and symptoms of Ebola hemorrhagic fever are not the same for all patients. Within a few days of becoming infected with the virus: high fever, headache, muscle aches, stomach pain, fatigue, diarrhea, sore throat, hiccups, rash, red and itchy eyes, vomiting blood, bloody diarrhea. Within one week of becoming infected with the virus: chest pain, shock, bleeding, blindness, and death. Researchers do not understand why some people are able to recover from Ebola hemorrhagic fever and others are not. However, it is known that patients who die usually have not developed a significant immune response to the virus at the time of death.

How is Ebola hemorrhagic fever clinically diagnosed?

Diagnosing Ebola hemorrhagic fever in an individual who has been infected only a few days is difficult because early symptoms, such as red and itchy eyes and a skin rash are nonspecific to the virus and are seen in other patients with diseases that occur much more frequently. If infection with Ebola virus is suspected, several laboratory tests should be done promptly. These include a blood film examination for malaria and a blood culture. If the suspected patient has bloody diarrhea, a stool culture should also be performed.

What laboratory tests are used to diagnose Ebola hemorrhagic fever?

Antigen-capture enzyme-linked immunosorbent assay (ELISA) testing, IgG ELISA, polymerase chain reaction (PCR), and virus isolation can be used to diagnose a case of Ebola hemorrhagic fever within a few days of the onset of symptoms. Persons tested later in the course of the disease or after recovery can be tested for IgM and IgG antibodies; the disease can also be diagnosed retrospectively in deceased patients by using immunohistochemistry testing, virus isolation, or PCR.

How is Ebola hemorrhagic fever treated?

There is no standard treatment for Ebola hemorrhagic fever. Currently, patients receive supportive therapy. This consists of balancing the patient's fluids and electrolytes, maintaining their oxygen status and blood pressure, and treating them for any complicating infections. During the Kikwit outbreak, eight patients were given blood of individuals who had been infected with Ebola virus but recovered. However, because the study size was small, and participant characteristics (including the fact that they were relatively young) predisposed them towards recovery, the efficacy of the treatment remains unknown.

How is Ebola hemorrhagic fever prevented?

The prevention of Ebola hemorrhagic fever in Africa presents many challenges. Because the identity and location of the natural reservoir of Ebola virus are unknown, there are few established primary prevention measures. If cases of the disease do appear, current social and economic conditions favor the spread of an epidemic within health care facilities. Therefore, health care providers must be able to recognize cases of Ebola hemorrhagic fever should one appear. They must also have the capability to perform diagnostic tests, and be ready to employ practical VHF isolation precautions, or barrier nursing techniques. These techniques include the wearing of protective clothing, such as masks, gloves, gowns, and goggles; the use of infection control measures, including complete equipment sterilization; and the isolation of Ebola hemorrhagic fever patients from contact with unprotected persons. The aim of all of these techniques is to avoid any person's contact with the blood or secretions of any patient. If a patient with Ebola hemorrhagic fever dies, it is equally important that direct contact with the body of the deceased patient be prevented. CDC has developed a set of tools to meet health care facilities' needs. In conjunction with the World Health Organization, CDC has developed practical, hospital-based guidelines that can help health care facilities recognize cases and prevent further hospital-based disease transmission using locally available materials and few financial resources. A similarly practical diagnostic test that uses tiny samples from patients' skin has been developed to retrospectively diagnose Ebola hemorrhagic fever in suspected case patients who have died.

What challenges remain for the control and prevention of Ebola hemorrhagic fever?

Scientists and researchers are faced with the challenges of developing additional diagnostic tools to assist in early diagnosis of the disease and ecological investigations of Ebola virus and the disease it causes. In addition, one of the research goals is to monitor suspected areas in order to determine the incidence of the disease. More extensive knowledge of the nature of the virus' reservoir and how it is spread must be acquired to prevent future outbreaks effectively.

Adapted from: 2002, Special Pathogens Branch, Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Public Health Service, U.S. Department of Health and Human Services. http://www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/ebola.htm (20 May 2003)

Filoviridae: Marburg Hemorrhagic Fever

What is Marburg hemorrhagic fever?

Marburg hemorrhagic fever is a rare, severe type of hemorrhagic fever, which affects both humans and non-human primates. Caused by a genetically unique zoonotic (that is, animal-borne) RNA virus of the filovirus family, its recognition led to the creation of this virus family. The four species of Ebola virus are the only other known members of the filovirus family. Marburg virus was first recognized in 1967, when outbreaks of hemorrhagic fever occurred simultaneously in laboratories in Marburg and Frankfurt, Germany and in Belgrade, Yugoslavia (now Serbia). A total of 37 people became ill; they included laboratory workers as well as several medical personnel and family members who had cared for them. The first people infected had been exposed to African green monkeys or their tissues. In Marburg, the monkeys had been imported for research and to prepare polio vaccine.

Where do cases of Marburg hemorrhagic fever occur?

Recorded cases of the disease are rare, and have appeared in only a few locations. While the 1967 outbreak occurred in Europe, the disease agent had arrived with imported monkeys from Uganda. No other case was recorded until 1975, when a traveler most likely exposed in Zimbabwe became ill in Johannesburg, South Africa – and passed the virus to his travelling companion and a nurse. 1980 saw two other cases, one in Western Kenya not far from the Ugandan source of the monkeys implicated in the 1967 outbreak. This patient's attending physician in Nairobi became the second case. Another human Marburg infection was recognized in 1987 when a young man who had traveled extensively in Kenya, including western Kenya, became ill and later died.

Where is Marburg virus found?

Marburg virus is indigenous to Africa. While the geographic area to which it is native is unknown, this area appears to include at least parts of Uganda and Western Kenya, and perhaps Zimbabwe. As with Ebola virus, the actual animal host for Marburg virus also remains a mystery. Both of the men infected in 1980 in western Kenya had traveled extensively, including making a visit to a cave, in that region. The cave was investigated by placing sentinel animals inside to see if they would become infected, and by taking samples from numerous animals and arthropods trapped during the investigation. The investigation yielded no virus. The sentinel animals remained healthy and no virus isolations from the samples obtained have been reported.

How do humans get Marburg hemorrhagic fever?

Just how the animal host first transmits Marburg virus to humans is unknown. However, as with some other viruses, which cause viral hemorrhagic fever, humans who become ill with Marburg hemorrhagic fever may spread the virus to other people. This may happen in several ways. Persons handling infected monkeys who come into direct contact with them or their fluids or cell cultures, have become infected. Spread of the virus between humans has occurred in a setting of close contact, often in a hospital. Droplets of body fluids, or direct contact with persons, equipment, or other objects contaminated with infectious blood or tissues are all highly suspect as sources of disease.

What are the symptoms of the disease?

After an incubation period of 5-10 days, the onset of the disease is sudden and is marked by fever, chills, headache, and myalgia. Around the fifth day after the onset of symptoms, a maculopapular rash, most prominent on the trunk (chest, back, stomach), may occur. Nausea, vomiting, chest pain, a sore throat, abdominal pain, and diarrhea then may appear. Symptoms become increasingly severe and may include jaundice, inflammation of the pancreas, severe weight loss, delirium, shock, liver failure, massive hemorrhaging, and multi-organ dysfunction. Because many of the signs and symptoms of Marburg hemorrhagic fever are similar to those of other infectious diseases, such as malaria or typhoid fever, diagnosis of the disease can be difficult, especially if only a single case is involved.

Which laboratory tests are used to diagnose Marburg hemorrhagic fever?

Antigen-capture enzyme-linked immunosorbent assay (ELISA) testing, IgM-capture ELISA, polymerase chain reaction (PCR), and virus isolation can be used to confirm a case of Marburg hemorrhagic fever within a few days of the onset of symptoms. The IgG-capture ELISA is appropriate for testing persons later in the course of disease or after recovery. The disease is readily diagnosed by immunohistochemistry, virus isolation, or PCR of blood or tissue specimens from deceased patients.

Are there complications after recovery?

Recovery from Marburg hemorrhagic fever may be prolonged and accompanied by orchitis, recurrent hepatitis, transverse myelitis or uvetis. Other possible complications include inflammation of the spinal cord, eye, parotid gland, or by prolonged hepatitis.

Is the disease ever fatal?

Yes. The case-fatality rate for Marburg hemorrhagic fever is between 23-25%.

How is Marburg hemorrhagic fever treated?

A specific treatment for this disease is unknown. However, supportive hospital therapy should be utilized. This includes balancing the patient's fluids and electrolytes, maintaining their oxygen status and blood pressure, replacing lost blood and clotting factors and treating them for any complicating infections. Sometimes treatment also has used transfusion of fresh-frozen plasma and other preparations to replace the blood proteins important in clotting. One controversial treatment is the use of heparin (which blocks clotting) to prevent the consumption of clotting factors. Some researchers believe the consumption of clotting factors is part of the disease process.

Who is at risk for the illness?

People who have close contact with a human or non-human primate infected with the virus are at risk. Such persons include laboratory or quarantine facility workers who handle non-human primates that have been associated with the disease. In addition, hospital staff and family members who care for patients with the disease are at risk if they do not use proper barrier nursing techniques.

How is Marburg hemorrhagic fever prevented?

Due to our limited knowledge of the disease, preventive measures against transmission from the original animal host have not yet been established. Measures for prevention of secondary transmission are similar to those used for other hemorrhagic fevers. If a patient is either suspected or confirmed to have Marburg hemorrhagic fever, barrier-nursing techniques should be used to prevent direct physical contact with the patient. These precautions include wearing of protective gowns, gloves, and masks; placing the infected individual in strict isolation; and sterilization or proper disposal of needles, equipment, and patient excretions.

What needs to be done to address the threat of Marburg hemorrhagic fever?

Marburg hemorrhagic fever is a very rare human disease. However, when it does occur, it has the potential to spread to other people, especially health care staff and family members who care for the patient. Therefore, increasing awareness among health-care providers of clinical symptoms in-patients that suggest Marburg hemorrhagic fever is critical. Better awareness can help lead to taking precautions against the spread of virus infection to family members or health-care providers. Improving the use of diagnostic tools is another priority. With modern means of transportation that give access even to remote areas, it is possible to obtain rapid testing of samples in disease control centers equipped with Biosafety Level 4 laboratories in order to confirm or rule out Marburg virus infection. A fuller understanding of Marburg hemorrhagic fever will not be possible until the ecology and identity of the virus reservoir are established. In addition, the impact of the disease will remain unknown until the actual incidence of the disease and its endemic areas are determined.

Adapted from: 2002, Special Pathogens Branch, Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Public Health Service, U.S. Department of Health and Human Services. http://www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/marburg.htm (20 May 2003)

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Bunyaviridae: Crimean-Congo Hemorrhagic Fever

Crimean-Congo hemorrhagic fever (CCHF) is a viral hemorrhagic fever of the *Nairovirus* group. Although primarily a zoonosis, sporadic cases and outbreaks of CCHF affecting humans do occur. The disease is endemic in many countries in Africa, Europe and Asia, and during 2001, cases or outbreaks were recorded in Kosovo, Albania, Iran, Pakistan, and South Africa.

The disease was first described in the Crimea in 1944 and given the name Crimean hemorrhagic fever. In 1969 it was recognized that the pathogen causing Crimean hemorrhagic fever was the same as that responsible for an illness identified in 1956 in the Congo, and linkage of the two place names resulted in the current name for the disease and the virus. CCHF is a severe disease in humans, with a high mortality rate. Fortunately, human illness occurs infrequently, although animal infection may be more common.

The geographical distribution of the virus, like that of its tick vector, is widespread. Evidence of CCHF virus has been found in Africa, Asia, the Middle East and Eastern Europe. Healthcare workers in endemic areas should be aware of the illness and the correct infection control procedures to protect themselves and their patients from the risk of nosocomial (hospital-acquired) infection.

CCHF Virus
The virus which causes CCHF is a *Nairovirus*, a group of related viruses forming one of the five genera in the *Bunyaviridae* family of viruses. All of the 32 members of the *Nairovirus* genus are transmitted by argasid or ixodid ticks, but only three have been implicated as causes of human disease: the Dugbe and Nairobi sheep viruses, and CCHF, which is the most important human pathogen amongst them.

CCHF Reservoirs and Vectors
The CCHF virus may infect a wide range of domestic and wild animals. Many birds are resistant to infection, but ostriches are susceptible and may show a high prevalence of infection in endemic areas. Animals become infected with CCHF from the bite of infected ticks.

A number of tick genera are capable of becoming infected with CCHF virus, but the most efficient and common vectors for CCHF appear to be members of the *Hyalomma* genus. Trans-ovarial (transmission of the virus from infected female ticks to offspring via eggs) and venereal transmission has been demonstrated amongst some vector species, indicating one mechanism, which may contribute to maintaining the circulation of the virus in nature. However, the most important source for acquisition of the virus by ticks is believed to be infected small vertebrates on which immature *Hyalomma* ticks feed. Once infected, the tick remains infected through its developmental stages, and the mature tick may transmit the infection to large vertebrates, such as livestock. Domestic ruminant animals, such as cattle, sheep and goats, are viremic (virus circulating in the bloodstream) for around one week after becoming infected.

Humans who become infected with CCHF acquire the virus from direct contact with blood or other infected tissues from livestock during this time, or they may become infected from a tick bite. The majority of cases have occurred in those involved with the livestock industry, such as agricultural workers, slaughterhouse workers and veterinarians.

Clinical Features
The length of the incubation period for the illness appears to depend on the mode of acquisition of the virus. Following infection via tick bite, the incubation period is usually one to three days, with a maximum of nine days. The incubation period following contact with infected blood or tissues is usually five to six days, with a documented maximum of 13 days.

Onset of symptoms is sudden, with fever, myalgia (aching muscles), dizziness, neck pain and stiffness, backache, headache, sore eyes and photophobia (sensitivity to light). There may be nausea, vomiting and sore throat early on, which may be accompanied by diarrhea and generalized abdominal pain. Over the next few days, the patient may experience sharp mood swings, and may become confused and aggressive. After two to four days, the agitation may be replaced by sleepiness, depression and lassitude, and the abdominal pain may localize to the right upper quadrant, with detectable hepatomegaly (liver enlargement).

Other clinical signs that emerge include tachycardia (fast heart rate), lymphadenopathy (enlarged lymph nodes), and a petechial rash (a rash caused by bleeding into the skin), both on internal mucosal surfaces, such as in the mouth and throat, and on the skin. The petechiae may give way to ecchymoses (like a petechial rash, but covering larger areas) and other hemorrhagic phenomena such as melaena (bleeding from the upper bowel, passed as altered blood in the feces), hematuria (blood in the urine), epistaxis (nosebleeds) and bleeding from the gums. There is usually evidence of hepatitis. The severely ill may develop hepatorenal (i.e., liver and kidney) and pulmonary failure after the fifth day of illness.

The mortality rate from CCHF is approximately 30%, with death occurring in the second week of illness. In those patients who recover, improvement generally begins on the ninth or tenth day after the onset of illness.

Diagnosis
Diagnosis of suspected CCHF is performed in specially equipped, high biosafety level laboratories. IgG and IgM antibodies may be detected in serum by enzyme-linked immunoassay (the "ELISA" or "EIA" methods) from about day six of illness. IgM remains detectable for up to four months, and IgG levels decline but remain detectable for up to five years.

Patients with fatal disease do not usually develop a measurable antibody response and in these individuals, as well as in patients in the first few days of illness, diagnosis is achieved by virus detection in blood or tissue samples. There are several methods for doing this. The virus may be isolated from blood or tissue specimens in the first five days of illness, and grown in cell culture. Viral antigens may sometimes be shown in tissue samples using immunofluorescence or EIA.

More recently, the polymerase chain reaction (PCR), a molecular method for detecting the viral genome, has been successfully applied in diagnosis.

Treatment
General supportive therapy is the mainstay of patient management in CCHF. Intensive monitoring to guide volume and blood component replacement is required.

The antiviral drug ribavirin has been used in treatment of established CCHF infection with apparent benefit. Both oral and intravenous formulations seem to be effective.

The value of immune plasma from recovered patients for therapeutic purposes has not been demonstrated, although it has been employed on several occasions.

Prevention and Control
Although an inactivated, mouse brain-derived vaccine against CCHF has been developed and used on a small scale in Eastern Europe; there is no safe and effective vaccine widely available for human use. The tick vectors are numerous and widespread and tick control with acaricides (chemicals intended to kill ticks) is only a realistic option for well-managed livestock production facilities.

Persons living in endemic areas should use personal protective measures that include avoidance of areas where tick vectors are abundant and when they are active (Spring to

Fall); regular examination of clothing and skin for ticks, and their removal; and use of repellents.

Persons who work with livestock or other animals in the endemic areas can take practical measures to protect themselves. These include the use of repellents on the skin (e.g. DEET) and clothing (e.g. permethrin) and wearing gloves or other protective clothing to prevent skin contact with infected tissue or blood.

When patients with CCHF are admitted to a hospital, there is a risk of nosocomial spread of infection. In the past, serious outbreaks have occurred in this way and it is imperative that adequate infection control measures be observed to prevent this disastrous outcome.

Patients with suspected or confirmed CCHF should be isolated and cared for using barrier-nursing techniques. Specimens of blood or tissues taken for diagnostic purposes should be collected and handled using universal precautions. Sharps (needles and other penetrating surgical instruments) and body wastes should be safely disposed of using appropriate decontamination procedures.

Healthcare workers are at risk of acquiring infection from sharps injuries during surgical procedures and, in the past, infection has been transmitted to surgeons operating on patients to determine the cause of the abdominal symptoms in the early stages of (at that moment undiagnosed) infection. Healthcare workers who have had contact with tissue or blood from patients with suspected or confirmed CCHF should be followed up with daily temperature and symptom monitoring for at least 14 days after the putative exposure.

Adapted from WHO Fact Sheet No 208
Revised November 2001
http://www.who.int/inf-fs/en/fact208.html (20 May 2003)

For more detailed information on CCHF, consult the following chapter: Nairovirus Infections, by R. Swanepoel, in Exotic Viral Infections, ed. J.S. Porterfield, London, 1995.
Helpful web-based resources include: All the Virology on the World-Wide Web, which provides information and links to numerous web-based virology sites.

Flaviviridae: Dengue Fever and Dengue Hemorrhagic Fever

Dengue is a mosquito-borne infection, which in recent years has become a major international public health concern. Dengue is found in tropical and sub-tropical regions around the world, predominantly in urban and semi-urban areas.

Dengue hemorrhagic fever (DHF), a potentially lethal complication, was first recognized in the 1950s during the dengue epidemics in the Philippines and Thailand, but today DHF affects most Asian countries and has become a leading cause of hospitalization and death among children in several of them.

There are four distinct, but closely related, viruses that cause dengue. Recovery from infection by one provides lifelong immunity against that serotype but confers only partial and transient protection against subsequent infection by the other three. There is good evidence that sequential infection increases the risk of more serious disease resulting in DHF.

Prevalence
The global prevalence of dengue has grown dramatically in recent decades. The disease is now endemic in more than 100 countries in Africa, the Americas, the Eastern Mediterranean, Southeast Asia and the Western Pacific. Southeast Asia and the Western Pacific are most seriously affected. Before 1970 only nine countries had experienced DHF epidemics, a number that had increased more than four-fold by 1995.

Some 2500 million people - two fifths of the world's population - are now at risk from dengue. WHO currently estimates there may be 50 million cases of dengue infection worldwide every year.

In 2001 alone, there were more than 609,000 reported cases of dengue in the Americas, of which 15,000 cases were DHF. This is greater than double the number of dengue cases which were recorded in the same region in 1995.

Not only is the number of cases increasing as the disease is spreading to new areas, but explosive outbreaks are occurring. In 2001, Brazil reported over 390,000 cases including more than 670 cases of DHF.

Some other statistics:
During epidemics of dengue, attack rates among susceptibles are often 40 – 50%, but may reach 80 – 90%.

An estimated 500,000 cases of DHF require hospitalization each year, of whom a very large proportion are children. At least 2.5% of cases die, although case fatality could be twice as high.

Without proper treatment, DHF case fatality rates can exceed 20%. With modern intensive supportive therapy, such rates can be reduced to less than 1%.

The spread of dengue is attributed to expanding geographic distribution of the four dengue viruses and of their mosquito vectors, the most important of which is the predominantly urban species *Aedes aegypti*. A rapid rise in urban populations is bringing ever-greater numbers of people into contact with this vector, especially in areas that are favorable for mosquito breeding, e.g., where household water storage is common and where solid waste disposal services are inadequate.

Transmission
Dengue viruses are transmitted to humans through the bites of infective female *Aedes* mosquitoes. Mosquitoes generally acquire the virus while feeding on the blood of an infected person. After virus incubation for 8-10 days, an infected mosquito is capable, during probing and blood feeding, of transmitting the virus, to susceptible individuals for the rest of its life. Infected female mosquitoes may also transmit the virus to their offspring by transovarial (via the eggs) transmission, but the role of this in sustaining transmission of virus to humans has not yet been delineated.

Humans are the main amplifying host of the virus, although studies have shown that in some parts of the world monkeys may become infected and perhaps serve as a source of virus for uninfected mosquitoes. The virus circulates in the blood of infected humans for two to seven days, at approximately the same time as they have fever; *Aedes* mosquitoes may acquire the virus when they feed on an individual during this period.

Characteristics
Dengue fever is a severe, flu-like illness that affects infants, young children and adults, but seldom causes death.

The clinical features of dengue fever vary according to the age of the patient. Infants and young children may have a non-specific febrile illness with rash. Older children and adults may have either a mild febrile syndrome or the classical incapacitating disease with abrupt onset and high fever, severe headache, pain behind the eyes, muscle and joint pains, and rash.

Dengue hemorrhagic fever is a potentially deadly complication that is characterized by high fever, hemorrhagic phenomena - often with enlargement of the liver—and in severe cases, circulatory failure. The illness commonly begins with a sudden rise in temperature accompanied by facial flush and other non-specific constitutional symptoms of dengue fever. The fever usually continues for two to seven days and can be as high as 40-41°C, possibly with febrile convulsions and hemorrhagic phenomena.

In moderate DHF cases, all signs and symptoms abate after the fever subsides. In severe cases, the patient's condition may suddenly deteriorate after a few days of fever; the temperature drops, followed by signs of circulatory failure, and the patient may rapidly go into a critical state of shock and die within 12-24 hours, or quickly recover following appropriate volume replacement therapy.

Treatment
There is no specific treatment for dengue fever. However, careful clinical management by experienced physicians and nurses frequently saves the lives of DHF patients. With appropriate intensive supportive therapy, mortality may be reduced to less than 1%. Maintenance of the circulating fluid volume is the central feature of DHF case management. [For detailed advice on managing patients with DHF see http://www.who.int/emc/diseases/ebola/Denguepublication/index.html] (20 May 2003)

Immunization
Vaccine development for dengue and DHF is difficult because any of four different viruses may cause disease, and because protection against only one or two dengue viruses could actually increase the risk of more serious disease. Nonetheless, progress is being made in the development of vaccines that may protect against all four dengue viruses. Such products may become available for public health use within several years.

Prevention and Control
At present, the only method of controlling or preventing dengue and DHF is to combat the vector mosquitoes.

In Asia and the Americas, *Aedes aegypti* breeds primarily in man-made containers like earthenware jars, metal drums and concrete cisterns used for domestic water storage, as well as discarded plastic food containers, used automobile tires and other items that collect rainwater. In Africa it also breeds extensively in natural habitats such as tree holes and leaf axils.

In recent years, *Aedes albopictus*, a secondary dengue vector in Asia, has become established in: the United States, several Latin American and Caribbean countries, in parts of Europe and in one African country. The rapid geographic spread of this species has been largely attributed to the international trade in used tires.

Vector control is implemented using environmental management and chemical methods. Proper solid waste disposal and improved water storage practices, including covering containers to prevent access by egg laying female mosquitoes are among methods that are encouraged through community-based programs.

The application of appropriate insecticides to larval habitats, particularly those which are considered useful by the householders, e.g. water storage vessels, prevent mosquito breeding for several weeks but must be re-applied periodically. Small, mosquito-eating fish and copepods (tiny crustaceans) have also been used with some success. During outbreaks, emergency control measures may also include the application of insecticides as space sprays to kill adult mosquitoes using portable or truck-mounted machines or even aircraft. However, the killing effect is only transient, variable in its effectiveness because the aerosol droplets may not penetrate indoors to microhabitats where adult mosquitoes are sequestered, and the procedure is costly and operationally very demanding. Regular monitoring of the vectors' susceptibility to the most widely used insecticides is necessary to ensure the appropriate choice of chemicals. Active monitoring and surveillance of the natural mosquito population should accompany control efforts in order to determine the impact of the program.

More information
For more information on dengue, including a list of those countries where outbreaks have occurred, please consult the World Health Organization's publication on the subject at the following website:
http://www.who.int/emc/diseases/ebola/Denguepublication/index.html. (20 May 2003)

Adapted from WHO Fact Sheet No 117, Revised April 2002,
http://www.who.int/inf-fs/en/fact117.html (20 May 2003)

For further information, please contact the Communications Office of the Director-General's Office, WHO Geneva, Tel (+41 22) 791 2090, Fax (+41 22) 791 4858; e-mail inf@who.int. All WHO Press Releases, Fact Sheets and Features can be obtained on Internet on the WHO home page: http://www.who.int/en (20 May 2003)

MISSOURI DEPARTMENT OF HEALTH

RECORD OF INVESTIGATION OF COMMUNICABLE DISEASE*

FOR CODING ONLY

County		City
Twnshp.		Disease
Hospital		Source
Physician		

Patient's Name			
Address	City	State	Zip Code
Birth / /	Sex ☐ M ☐ F	Race ☐ W ☐ N ☐ Other	County of Residence
Parent's Name If Not Adult		Phone	
Hospitalized ☐ Yes ☐ No	Hospital Name		Date of Onset

Physician's Name	Phone Number
Address	Date
Previous Address (if significant)	Date Moved
Place Employed or School Attended	Occupation

Date Reported	How did you first learn of this case?	Date

Disease ______________________ ☐ Confirmed or ☐ Suspected } at beginning of investigation.

Chief Clinical Symptoms with Dates: ______

Treatment (type, amount, dates): ______

DIAGNOSTIC LABORATORY TESTS ON PATIENT

Type of Specimen	Date Collected	Result	Name of Laboratory

Are there other associated cases? ______ If yes, how many, and how associated? ______

Household Sanitation: ☐ Good ☐ Fair ☐ Poor

Milk Supply ______

Water Supply ______

(Continued on reverse side)

* Special forms should be used for investigations of Diphtheria (CD 2A), Encephalitis or Meningitis (CD 2B), Enteric Infections (CD 2C), and Foodborne Outbreaks (CD 2D).

Other Pertinent Epidemiological Data (exposure to birds and animals, insect bites, vaccination, travel, etc.): ______

CONTACTS (Household and Other)

Name and Address	Age / Sex	Relation to Patient	Similar Illness? Onset Date	Laboratory Specimen	Date Collected	Result

Narrative and Follow-up Notes: ______

Probable Source ______

☐ Recovered ☐ Died Date of Death ______ Cause of Death ______

Investigated by ______ Final Diagnosis ______

Name of Agency ______ Date ______